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LETTER TO THE EDITOR

First Description of IncX3 Plasmids Carrying $bla_{OXA-181}$ in *Escherichia coli* Clinical Isolates in Burkina Faso

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Carbapenemase-producing *Enterobacteriaceae* (CPE) have been increasingly reported worldwide. The few studies available on CPE epidemiology in West and East Africa highlight the identification of carbapenemases in Cameroon (NDM-4), Kenya (NDM-1), Sierra Leone (VIM and DIM-1), Senegal (OXA-48), and Tanzania (KPC, IMP, OXA-48, VIM, and NDM) (1). Although bla_{OXA-48} genes are widely spread in North Africa, bla_{OXA-48} derivatives have been rarely reported in Africa. Indeed, $bla_{OXA-163}$ was detected only twice in Egypt and $bla_{OXA-181}$ (a point mutant analogue of OXA-48) only once in South Africa (1). Here, we describe the first four cases of *Escherichia coli* carrying the $bla_{OXA-181}$ gene in Burkina Faso.

Four *E. coli* strains (Table 1) were isolated from four patients in two hospitals in Ouagadougou, Burkina Faso. Carbapenem MICs, determined using the Etest (bioMérieux), were 1 to 1.5 mg/liter, 0.125 to 0.75 mg/liter, and 0.25 to 0.5 mg/liter for ertapenem, doripenem, and imipenem, respectively (Table 1). Three patients received antibiotics before strain isolation (Table 1). None of the patients reported recent travel outside Burkina Faso. Multiplex PCR and DNA sequencing targeting the most prevalent extended-spectrum-β-lactamase (ESBL)- and carbapenemase-encoding genes (2, 3) revealed the presence of $bla_{CTX-M-15}$ and of $bla_{OXA-181}$ in the four isolates. No other carbapenemase-encoding gene (corresponding to NDM, VIM, IMP, and KPC) was detected. Multilocus sequence typing (MLST) (http://bigsdb.web.pasteur.fr/) showed that the four strains belonged to new sequence type (ST) ST692, which is described here for the first time. Enterobacterial repetitive intergenic consensus sequence PCR (ERIC-PCR) (4) patterns (see Fig. S1 in the supplemental material) and the variable-number tandem-repeat (VNTR) (5) profile determined on the basis of analysis of 7 polymorphic loci (6-1-5-8-3-5-1; see Table 1) confirmed the genetic links among the four *E. coli* strains. However, the review of medical records indicated that the four patients were hospitalized in different structures (hospitals and wards). Although there was no relationship or housing shared between the patients, these data support the hypothesis of infections by the same multidrug-resistant clone circulating in these hospitals or in the general community.

Plasmid DNA was extracted by alkaline lysis and subsequently analyzed by gel electrophoresis as previously described (6). Comparative analysis was carried out using reference plasmids RP4 (54 kb), pCFF04 (85 kb), and pIP173 (126.8 kb) and showed two different plasmids of ca. 120 kb and ca. 54 kb, respectively, in each strain.

Mating experiments performed using azide-resistant *E. coli* strain J53 as a recipient under various conditions were unsuccessful. Plasmid DNA was extracted using a QIAprep Spin Miniprep kit (Qiagen) and transferred by electroporation into *E. coli* DH10B (Invitrogen, Cergy-Pontoise, France). The $bla_{OXA-181}$-carrying transformants showed ertapenem and imipenem MICs of 0.38 to 0.5 mg/liter and 0.5 to 0.75 mg/liter, respectively. Analysis by plasmid relaxase gene typing (7) and PCR-based replicon typing (8) identified IncX3-type relaxase and ColE-type replication initiation genes, respectively, in the transformants. Alkaline lysis of transformants and subsequent electrophoresis showed that these genes were carried by the ca. 54-kb plasmid. As a $bla_{OXA-181}$-carrying IncX3 plasmid was recently identified in *E. coli* in China (9), PCR mapping was carried out in the four strains and their respective transformants with primers designed using plasmid pOXA181_EC14828 as the template (GenBank accession number KP400525). All primers used for PCR mapping are reported in Table S1 in the supplemental material. PCR mapping gave similar results in all four *E. coli* strains. DNA regions surrounding the $bla_{OXA-181}$ gene are detailed in Fig. 1 and showed that $bla_{OXA-181}$ was part of the Tn*2013* transposon, as previously described (10). The same genetic context was recovered in all six $bla_{OXA-181}$-surrounding sequences available in the GenBank database (GenBank accession numbers KP400525, AB972272, JN205800, NZ_JRKW01000020, JQ996150, and KT005457) (11, 12). The *repA1* gene (encoding a ColE-type replication initiation protein) was downstream of Tn*2013*. This replicase gene was also found on plasmids pKP3-A (JN205800) and pMR3-OXA181 (NZ_JRKW01000020) that belong to the ColE and IncN incom-

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TABLE 1 Clinical and microbiological characteristics of the four $bla_{OXA-181}$-producing *E. coli* isolates and their respective transformants and of *E. coli* J53[a]

Characteristic	Result								
	EC187	EC187 (T)	EC292	EC292 (T)	EC309	EC309 (T)	EC327	EC327 (T)	*E. coli* J53
Patient	F, 12 yrs old		M, 2 yrs old		F, 65 yrs old		F, 21 yrs old		
Origin	Urine		Suppuration		Suppuration		Urine		
Clinical symptom or diagnosis	Dysuria		Abdominal pain		Peritonitis		Unknown		
Use of antibiotics in the previous 3 mo	None reported		CFM, CRO, GE		AMC, GE		CRO, GE		
MLST	ST692		ST692		ST692		ST692		
VNTR[b]	6-1-5-8-3-5-1		6-1-5-8-3-5-1		6-1-5-8-3-5-1		6-1-5-8-3-5-1		
MIC (mg/liter)									
Ertapenem	1	0.5	1.5	0.5	1.5	0.5	1.5	0.38	0.06
Doripenem	0.125	ND	0.25	ND	0.25	ND	0.75	ND	ND
Imipenem	0.25	0.5	0.5	0.75	0.38	0.5	0.38	0.5	0.25
Associated resistance									
ESBL	CTX-M-15	None	CTX-M-15	None	CTX-M-15	None	CTX-M-15	None	
Non-β-lactam resistance	CIP, GE, SXT, TE	ND	CIP, GE, SXT, TE	ND	CIP, GE, SXT, TE	ND	CIP, GE, SXT, TE	ND	

[a] (T), transformant; F, female; M, male; ND, not determined; AMX, amoxicillin; AMC, amoxicillin-clavulanic acid (co-amoxiclav); CFM, cefixime; CIP, ciprofloxacin; CRO, ceftriaxone; GE, gentamicin; SXT, sulfamethoxazole-trimethoprim; TE, tetracycline.
[b] Data represent CNV1, CNV2, CNV3, CNV4, CNV7, CNV14, and CNV15.

patibility groups, respectively. This suggests that $bla_{OXA-181}$ might have come from a ColE-type scaffold. Fluoroquinolone resistance gene *qnrS1* was also detected downstream of $bla_{OXA-181}$ (Fig. 1). An IncX3-specific backbone was recovered at the 5′ extremity of $bla_{OXA-181}$-surrounding regions and included, in addition to the *repB* replicase gene, the *parA* partition gene (13) and the *umuD* gene involved in SOS mutagenesis (14). Large-scale PCR mapping targeting various plasmid regions, including transfer, replication,

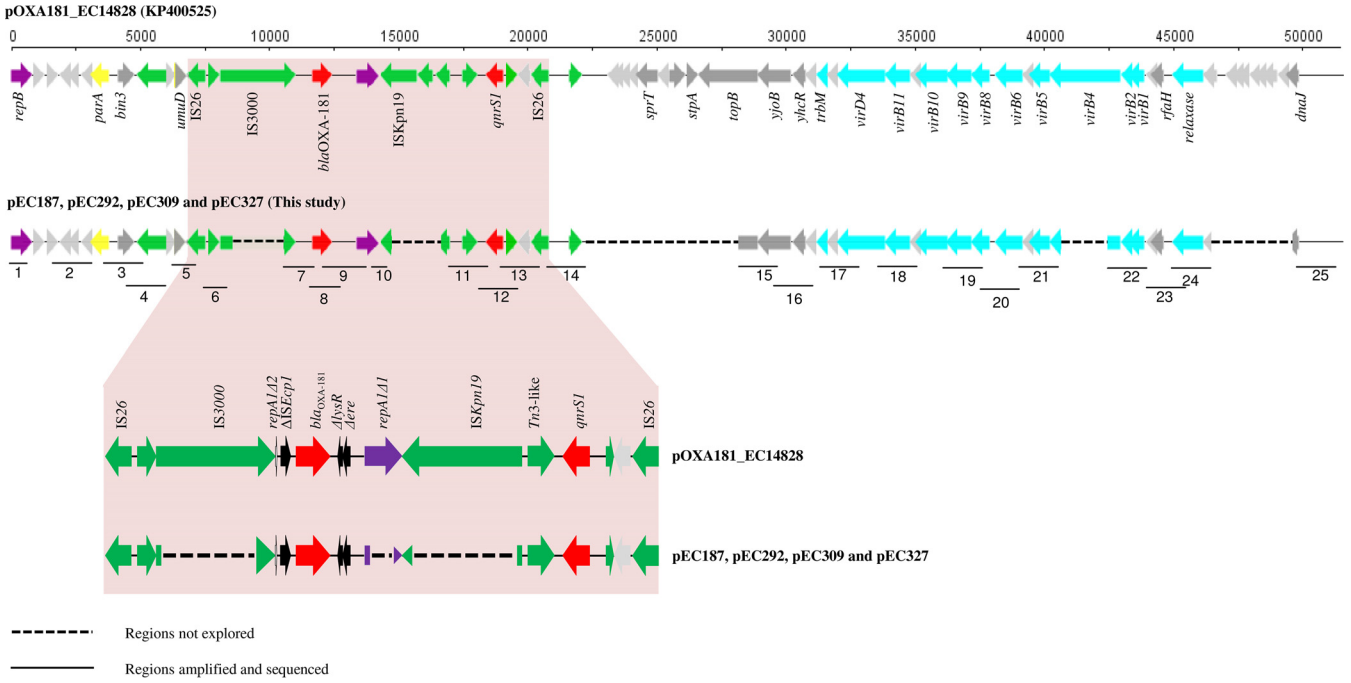

FIG 1 Genetic map of the four plasmids harboring $bla_{OXA-181}$ described in this report. Purple arrows represent the replicase genes. Light-gray arrows represent genes encoding hypothetical proteins. Yellow arrows represent genes encoding partition systems. Dark-gray arrows represent accessory genes. Green arrows represent transposase-encoding genes and insertion sequences. Red arrows represent antimicrobial resistance genes. Blue arrows represent genes implicated in plasmid transfer. The genetic context of $bla_{OXA-181}$ is visually extended at the bottom. Plasmid pOXA181_EC14828 was harbored by an *E. coli* isolate in China (GenBank accession no. KP400525) and was used as a model to map the four $bla_{OXA-181}$-carrying plasmids described in this report. Thin black lines represent the 25 oligonucleotide pairs used for PCR mapping in all four plasmids. All amplicons were fully sequenced and displayed 100% identity to those of plasmid pOXA181_EC14828.

and partition systems, was also performed and covered a total of 29,569 bp, which amounts to ca. 55% coverage compared to the estimated size of the plasmid (Fig. 1; see also Table S1 in the supplemental material). All PCR products displayed 100% identity to those encoded by the respective regions of plasmid pOXA181_EC14828 (Fig. 1).

Since the first description in Indian hospitals in 2011, OXA-181-positive *Enterobacteriaceae* have been reported worldwide (1, 11). Their emergence in West Africa in IncX3 plasmids is of particular concern because these plasmids mediate the spread of carbapenemases in *Enterobacteriaceae* (15, 16). Moreover, a recent study found an IncX3 plasmid harboring $bla_{\text{OXA-181}}$ in a *Klebsiella variicola* isolate in fresh vegetables imported to Switzerland from Asia (12). This plasmid, named pKS22 (KT005457), is highly similar to pOXA181_EC14828 (100% coverage and 99% identity) and therefore to the four IncX3 plasmids described in our report. The presence of highly similar IncX3 plasmids in Asia, Africa, and Europe might suggest the epidemic potential of the members of this plasmid lineage and their role in worldwide dissemination of OXA-181.

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